

FIG. 1

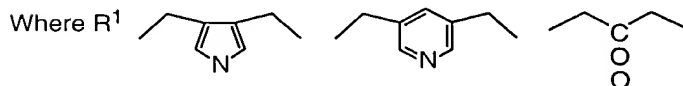
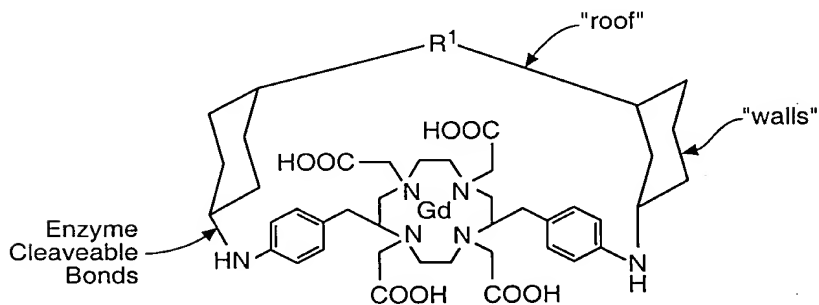


FIG. 2

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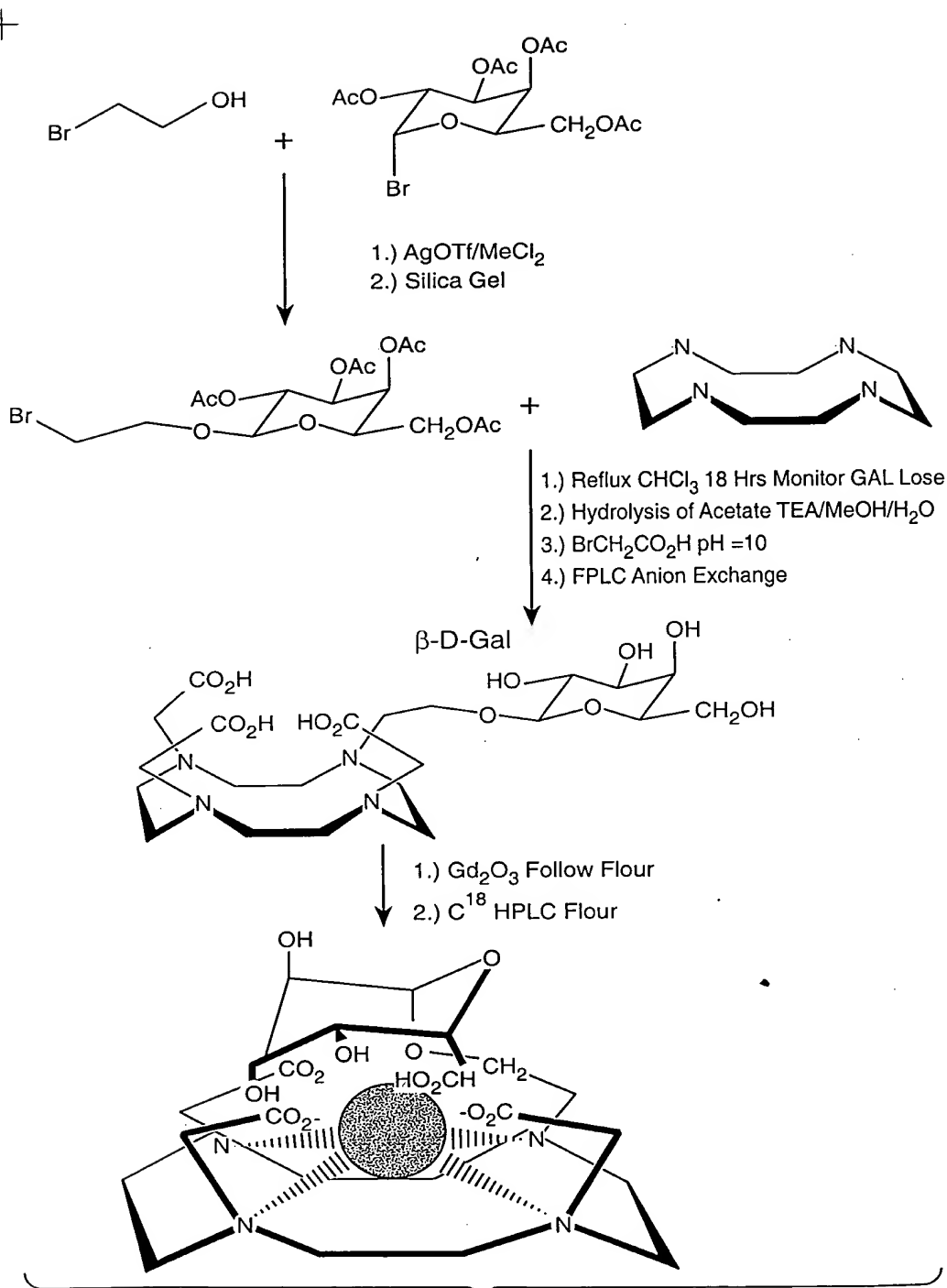
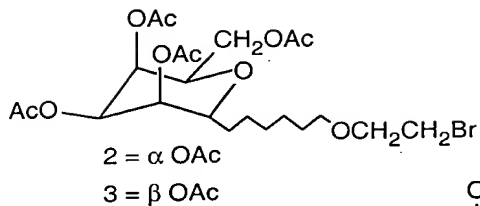
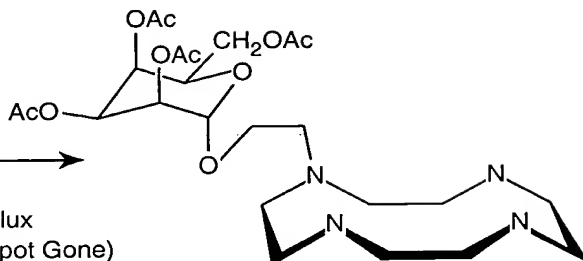


FIG. 3



1 + 2

CHCl_3
48 Hrs Reflux
T.L.C. (2 Spot Gone)



5

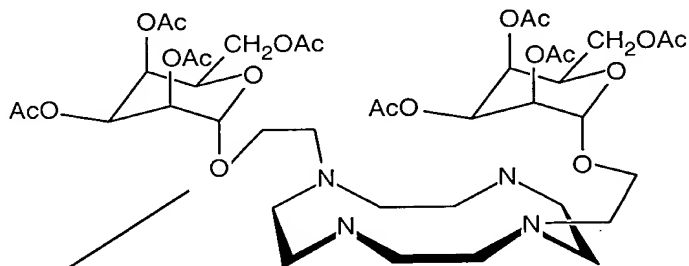
12 = α OH

(7 = β)

13 = β OH



1



6

(8 = β)

~2:1 6:5

Silica
4:1 $\text{CHCl}_3/\text{MeOH}$

8 \longrightarrow

- 1.) Hydrolysis Of Acetate
TCA/MeOH / H_2O
- 2.) $\text{BrCH}_2\text{CO}_2\text{H}$ pH = 10
- 3.) FPLC Cation Exchange
pH = 2 Acetic Acid Gradient

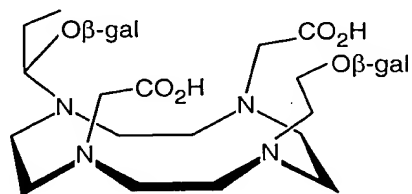
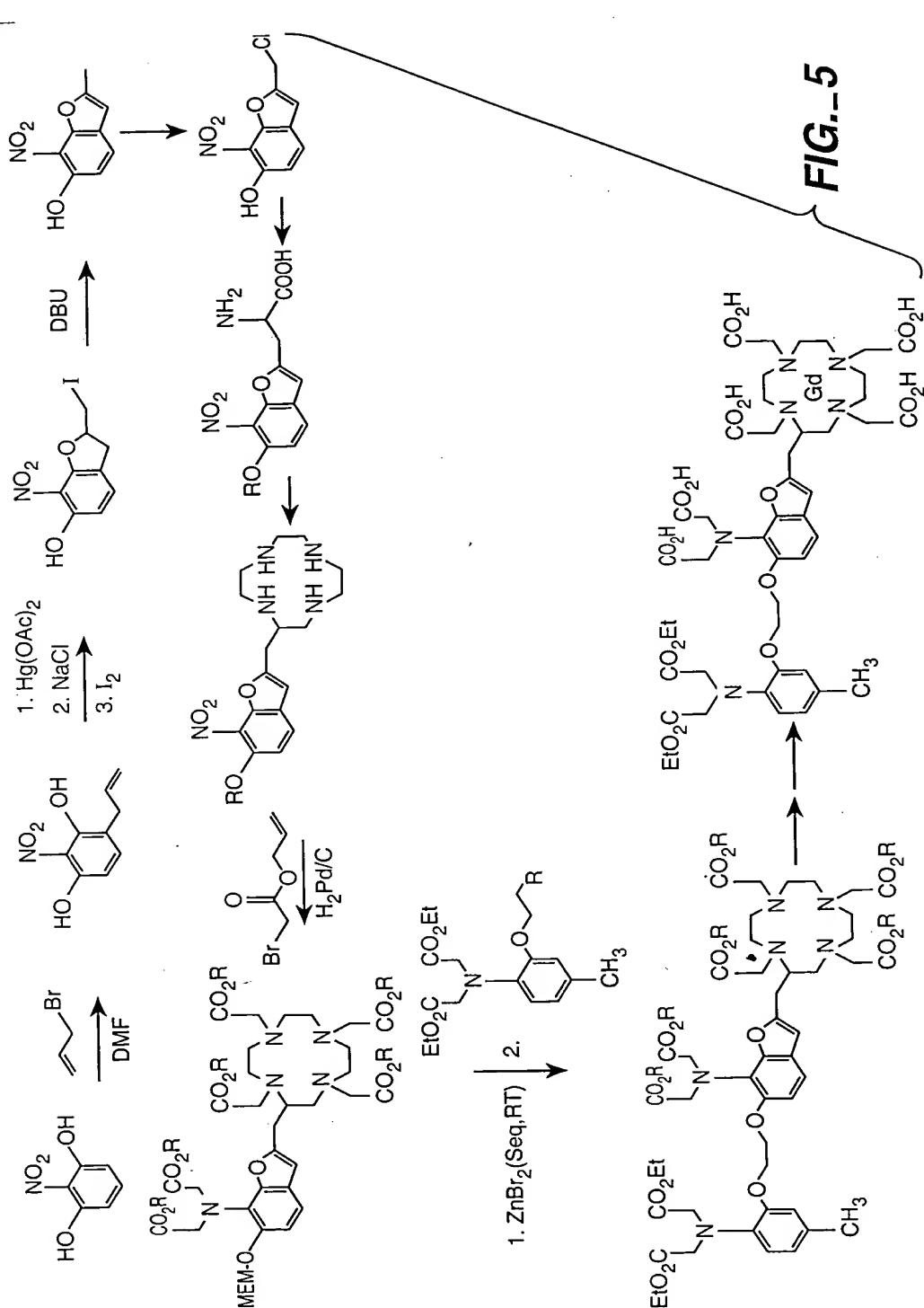
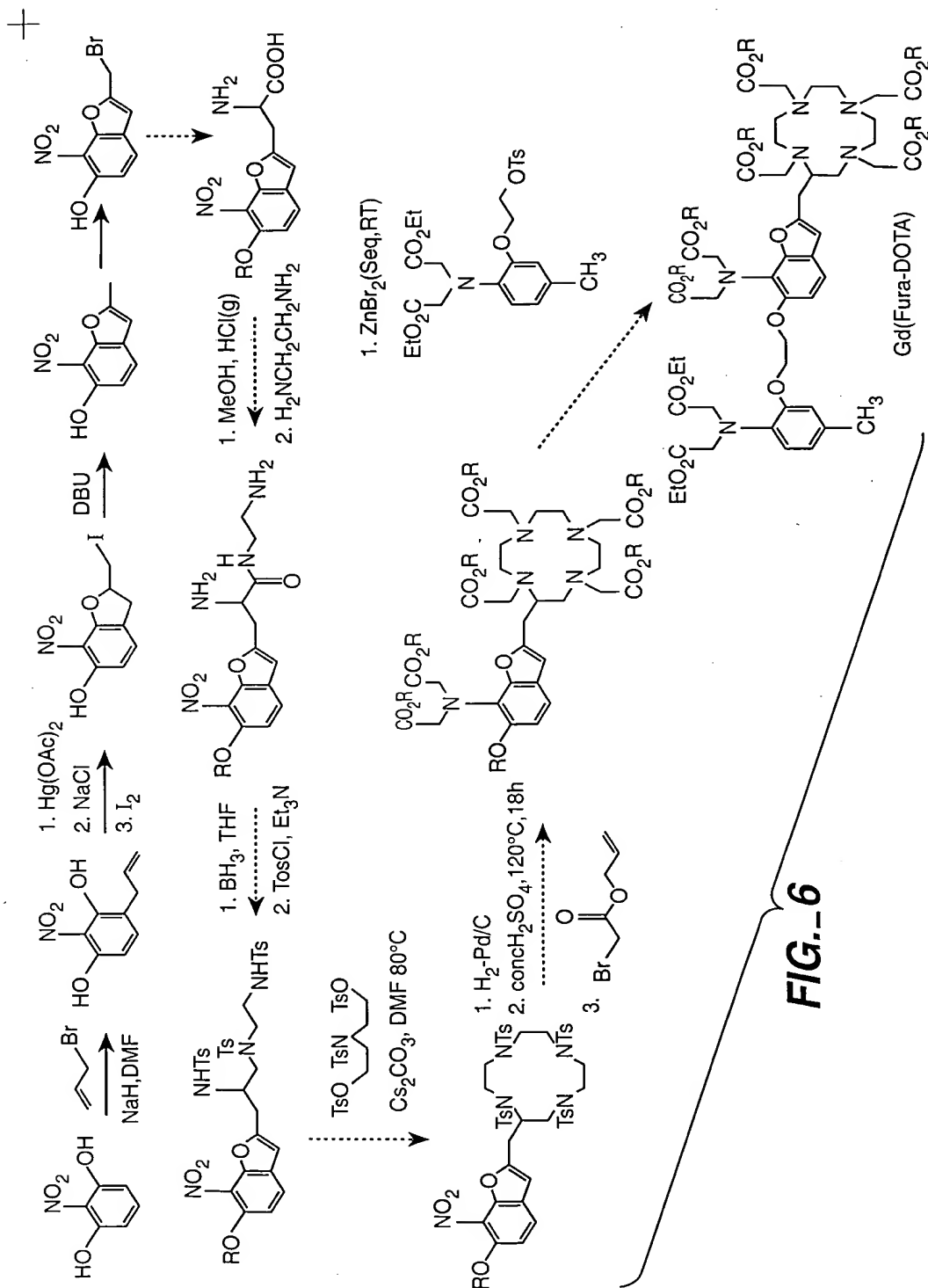


FIG._4





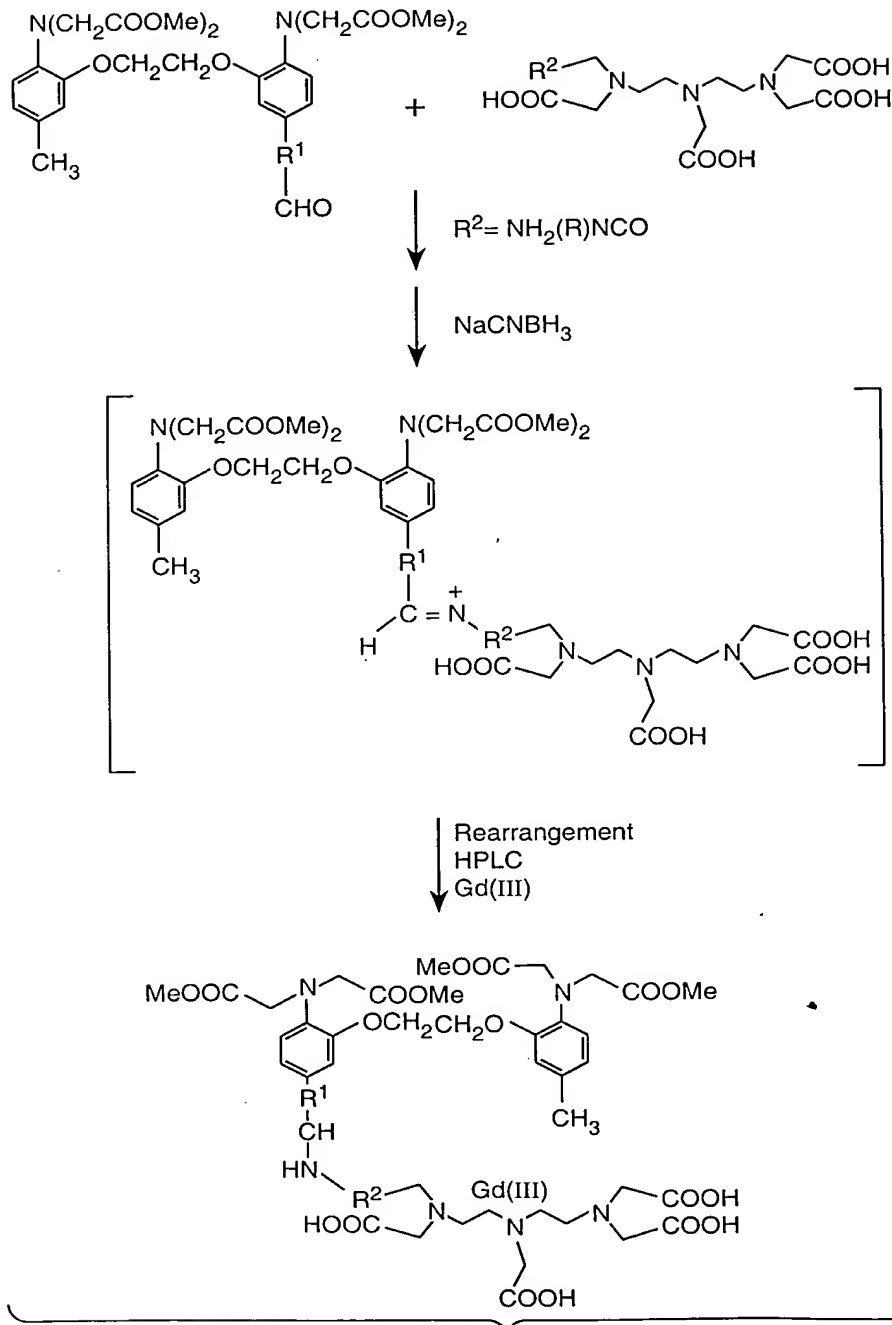


FIG. 7

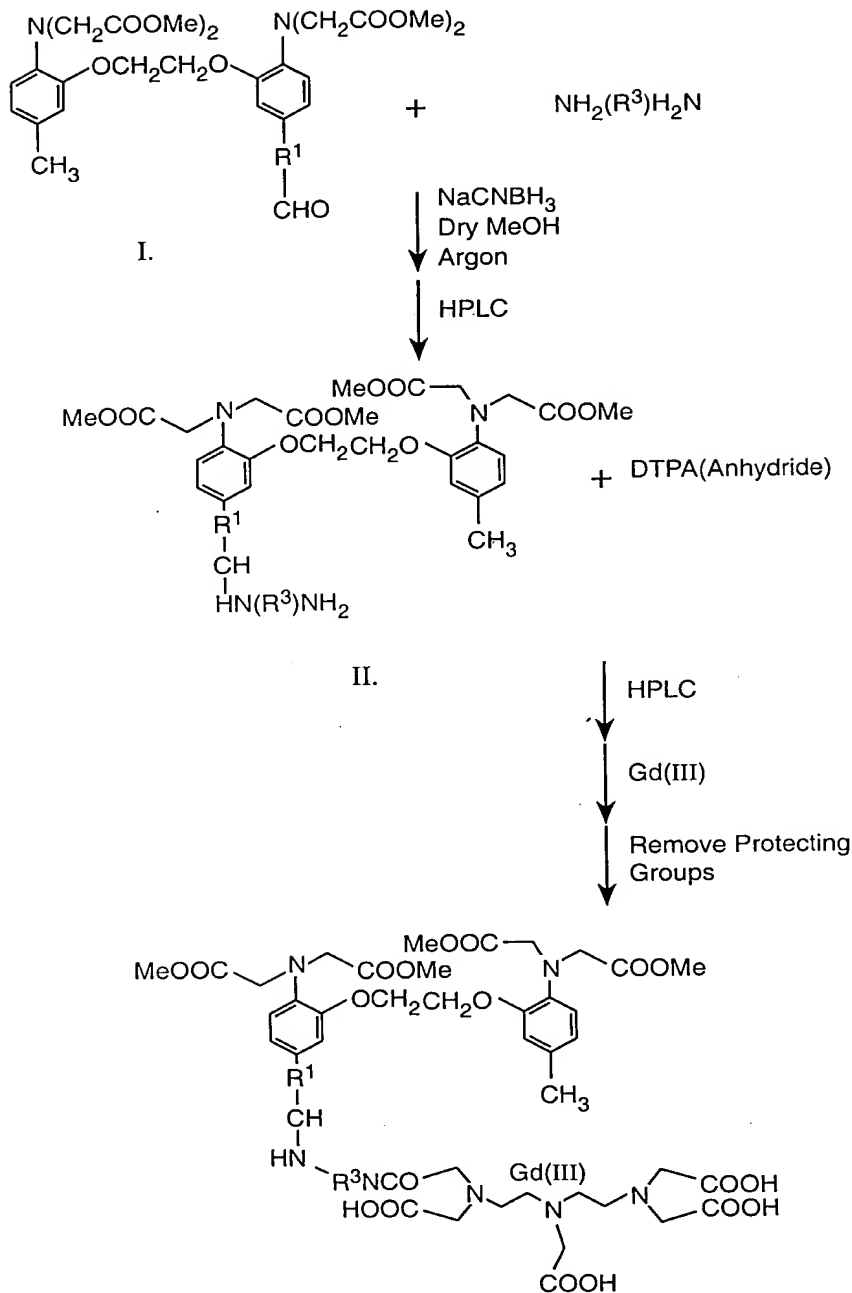


FIG. 8

T04250*2FS99860

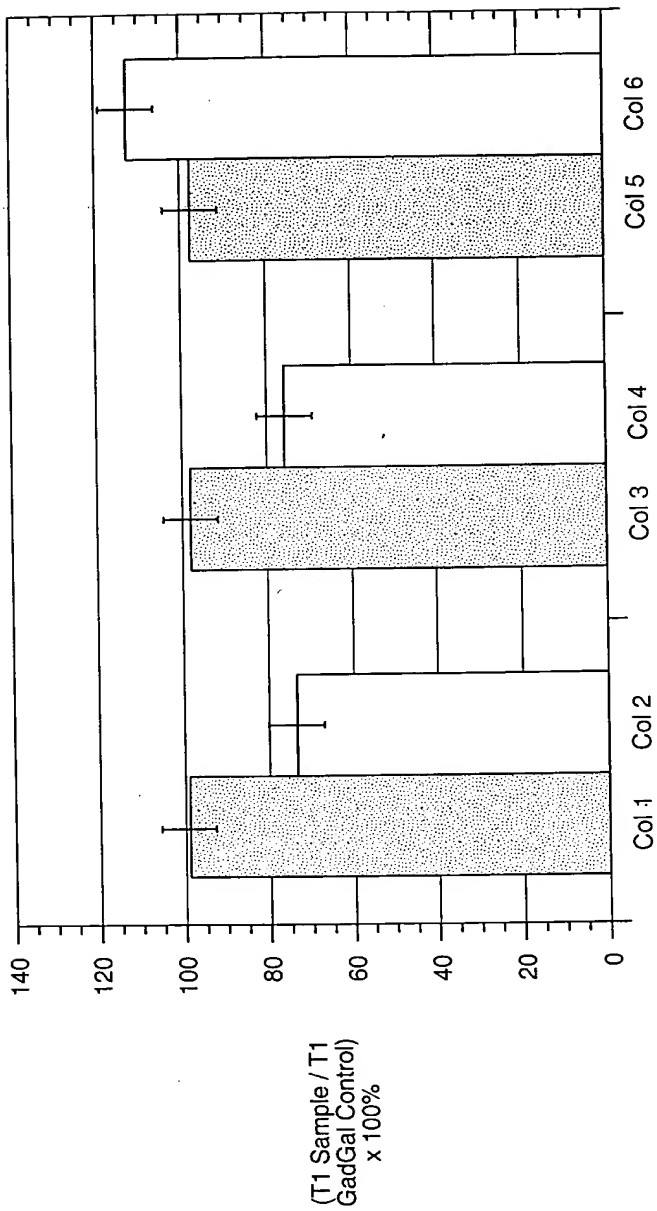
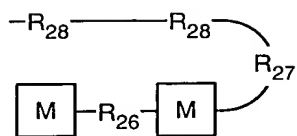
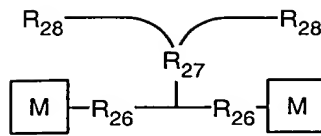
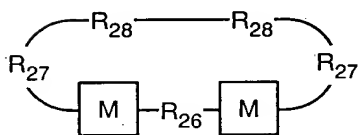
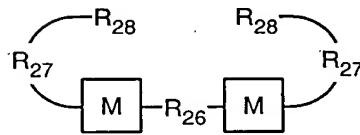
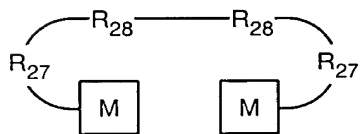
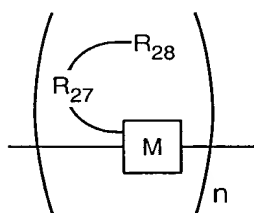
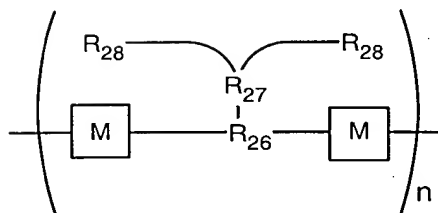
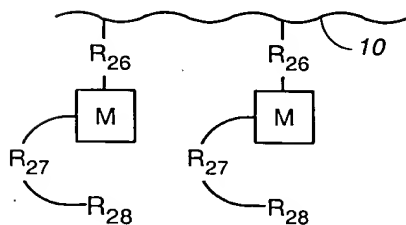
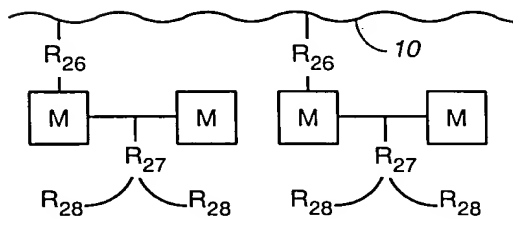


FIG._9

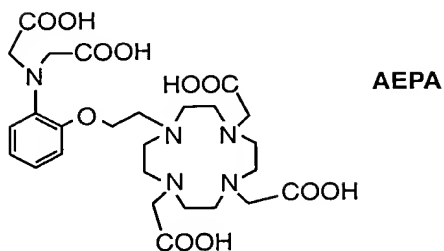
+

**FIG. 10A****FIG. 10B****FIG. 10C****FIG. 10D****FIG. 10E****FIG. 10F****FIG. 10G****FIG. 10H****FIG. 10I**

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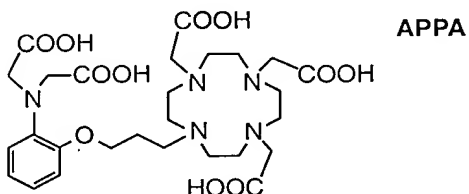
+

+



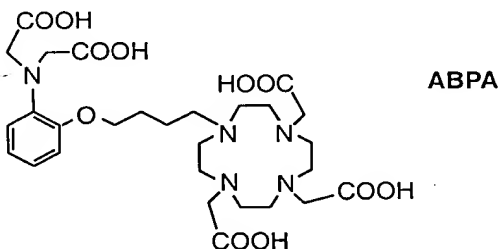
1-o-aminophenoxy-2-(cyclen)ethane-N,N,N',N'',N'''-pentaacetic acid

FIG._11A



1-o-aminophenoxy-3-(cyclen)propane-N,N,N',N'',N'''-pentaacetic acid

FIG._11B



1-o-aminophenoxy-4-(cyclen)butane-N,N,N',N'',N'''-pentaacetic acid

FIG._11C

09866512-052401

+

+

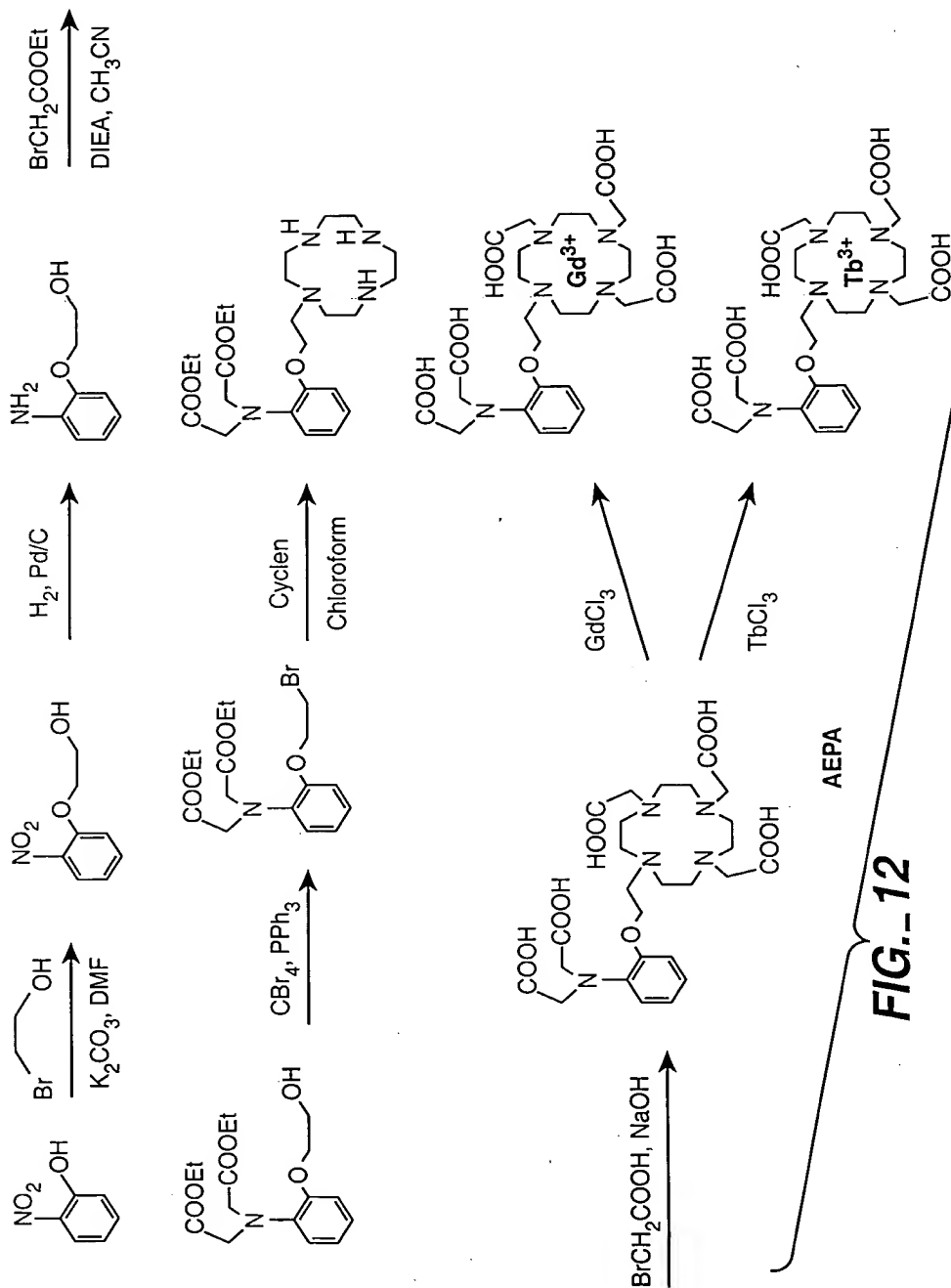
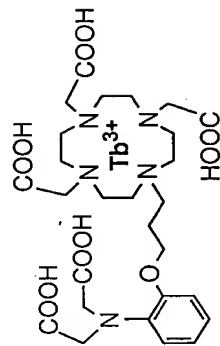
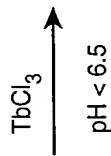
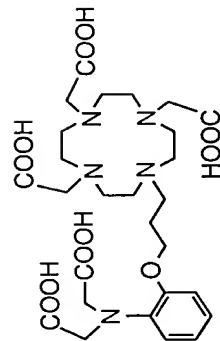
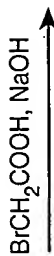
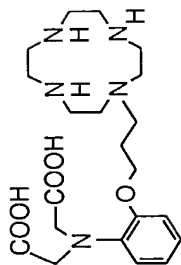
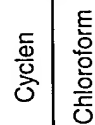
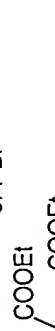
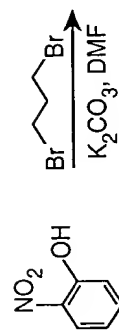
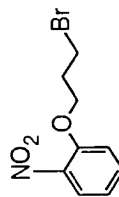
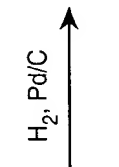
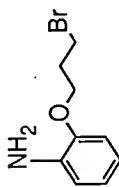
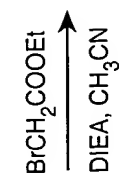


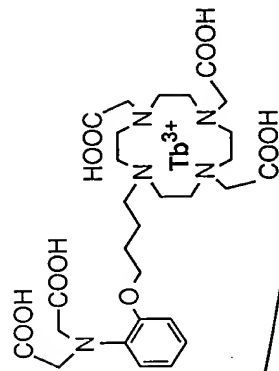
FIG. 12

+

+



APPA-Tb³⁺



or ABPA-Tb³⁺

(from dibromobutane)

FIG. 13

+

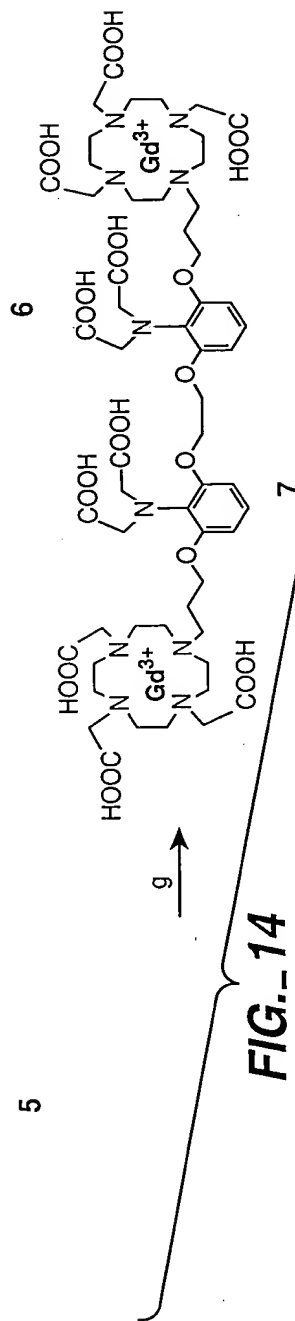
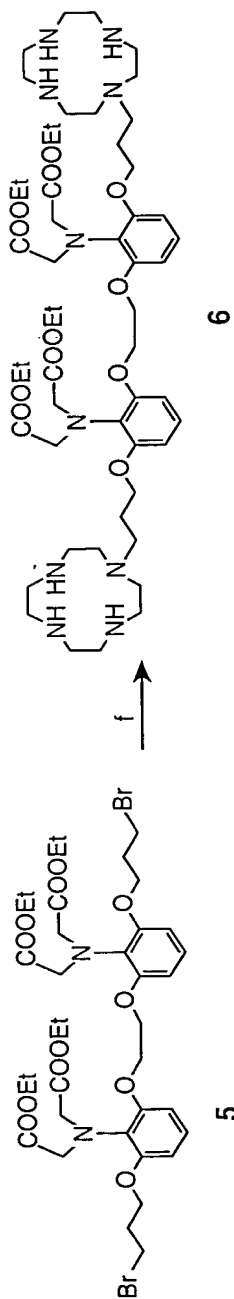
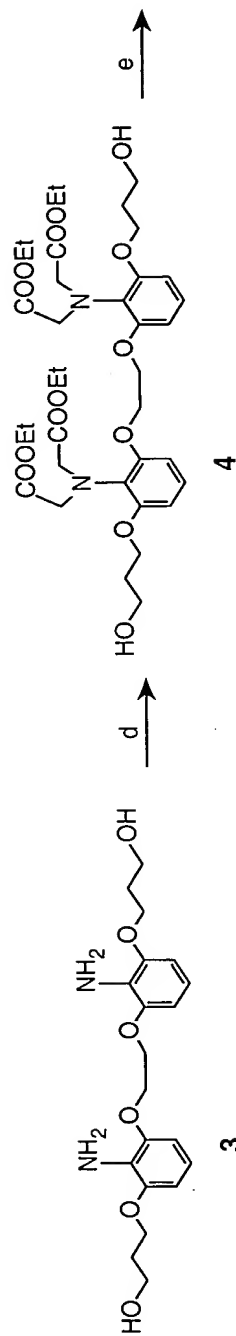
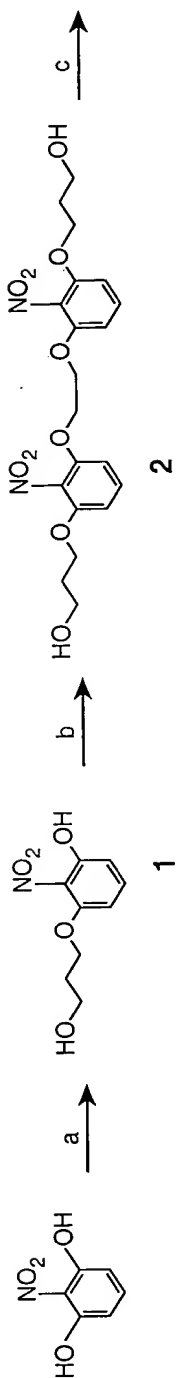


FIG. 14

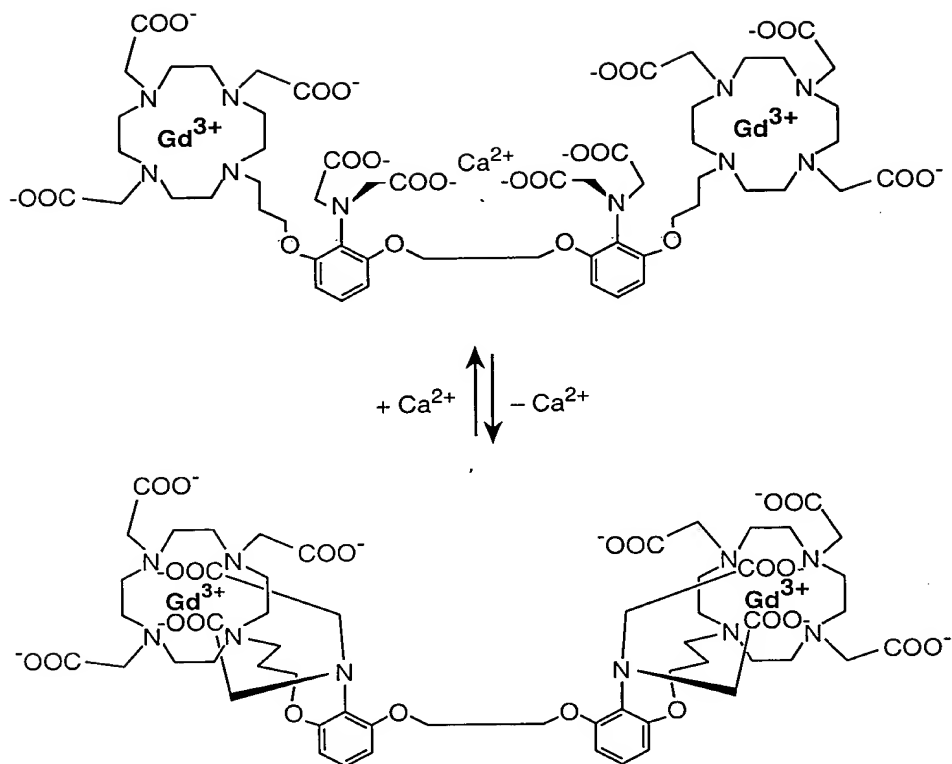


FIG. 15

104250 21599860

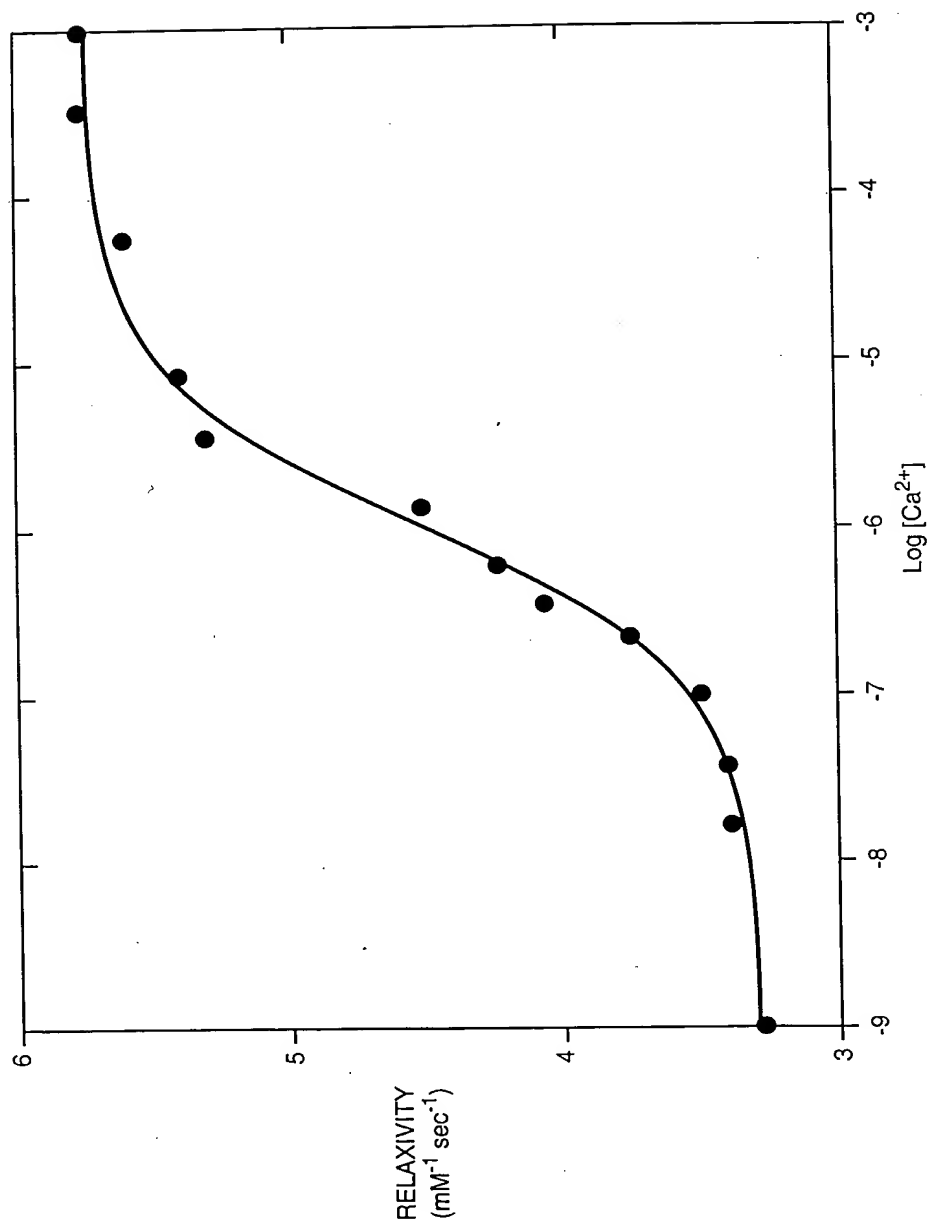


FIG. 16

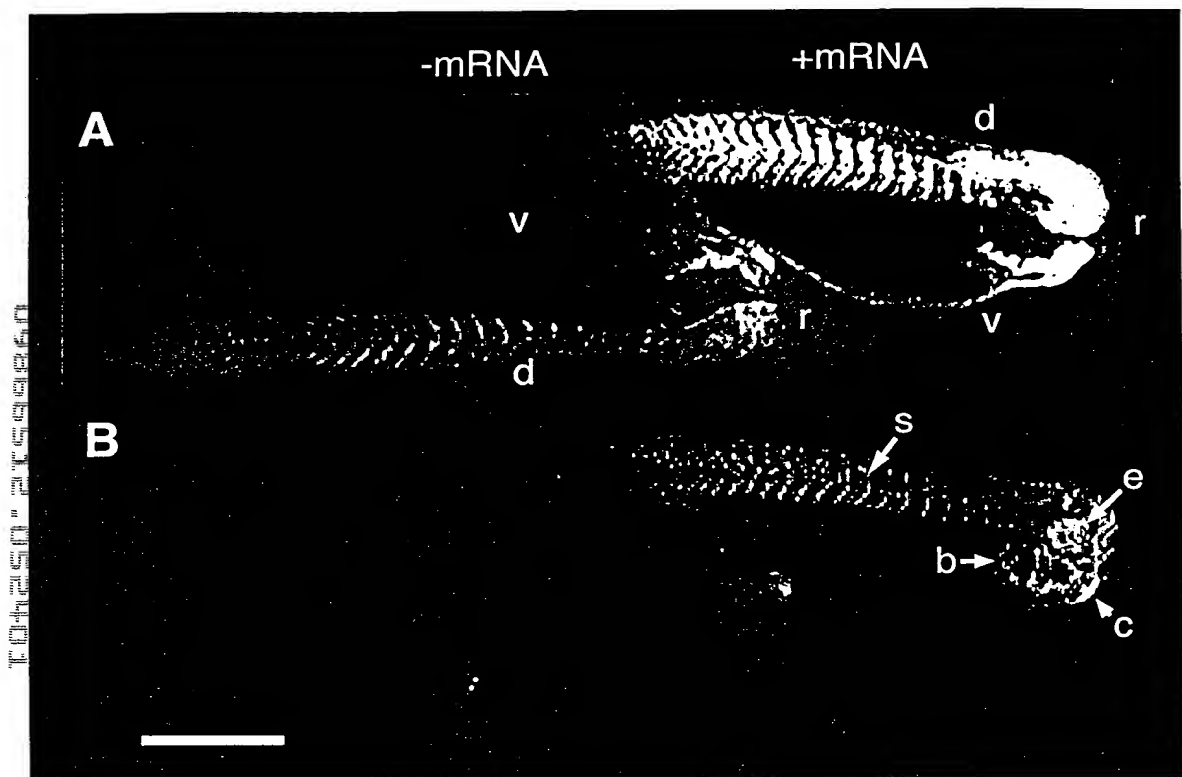


FIG._17

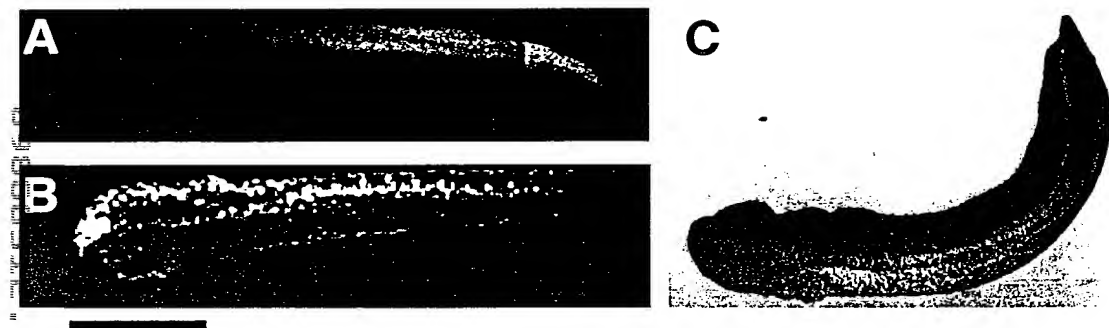


FIG._18

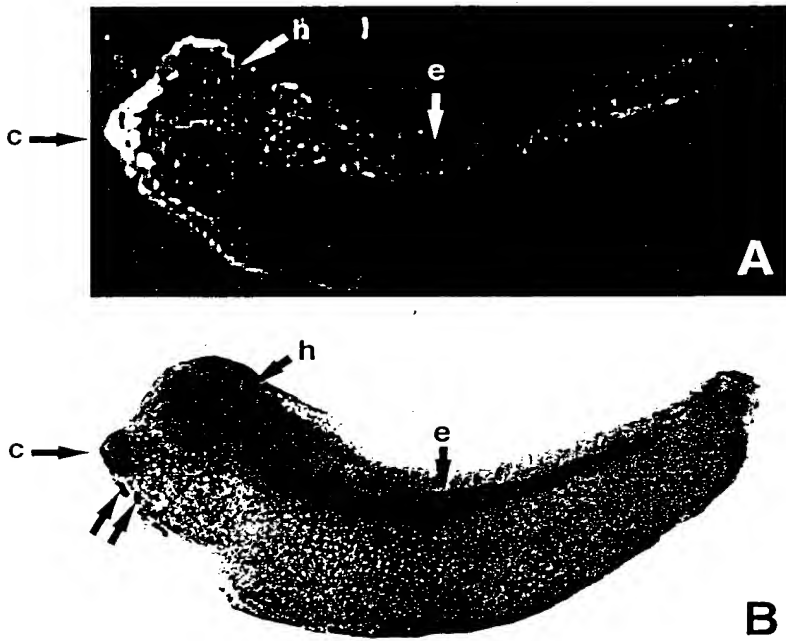


FIG._19

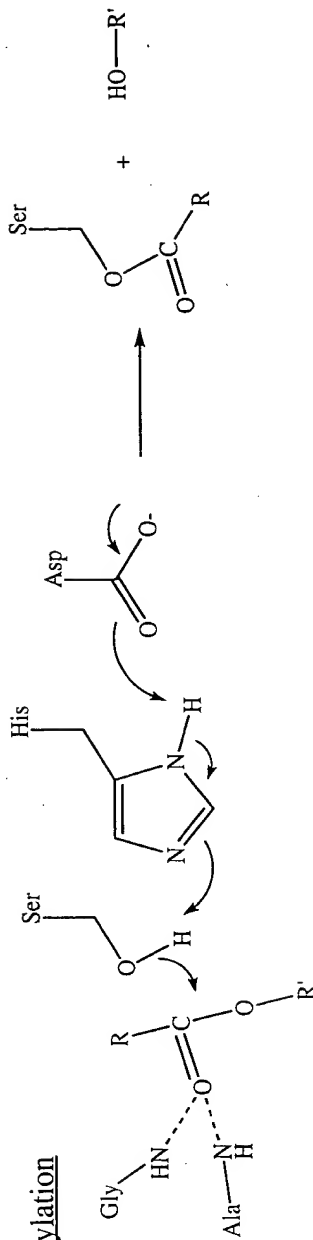
Properties of Carboxylesterases:

1. Efficient cleavage of Ester functional groups

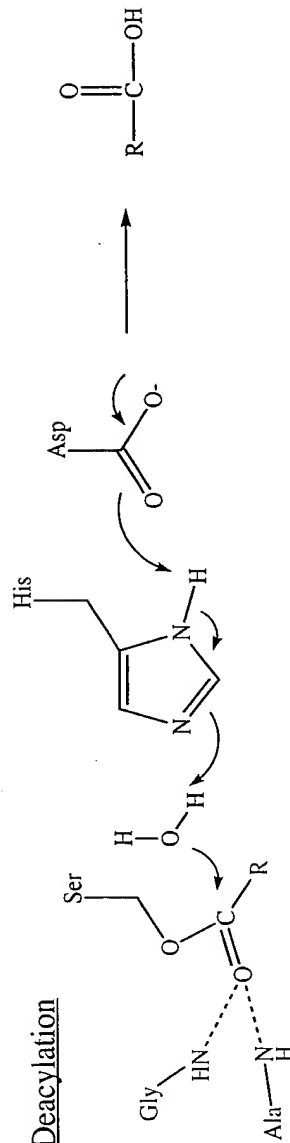


2. Belongs to the family of Ser-His-Asp active site enzymes (serine protease)

Acylation

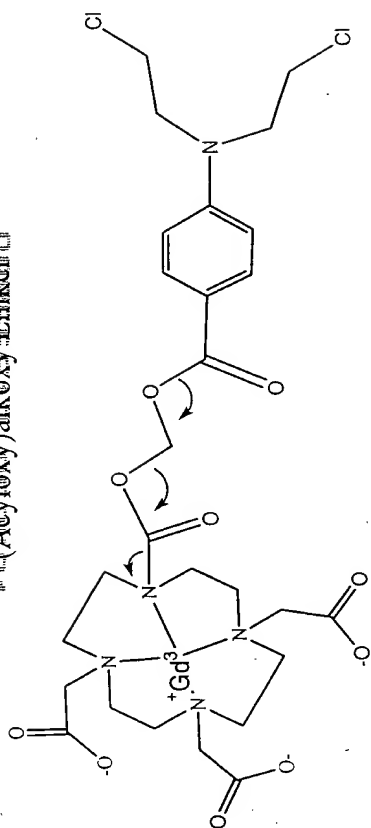


Deacylation

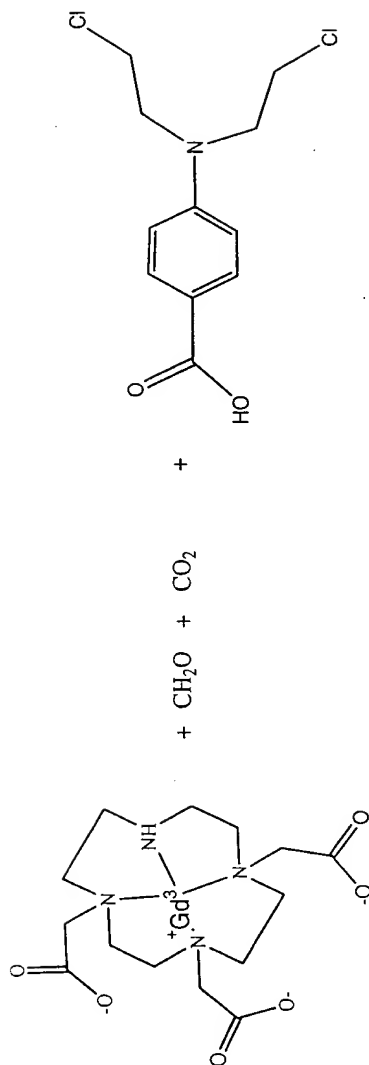


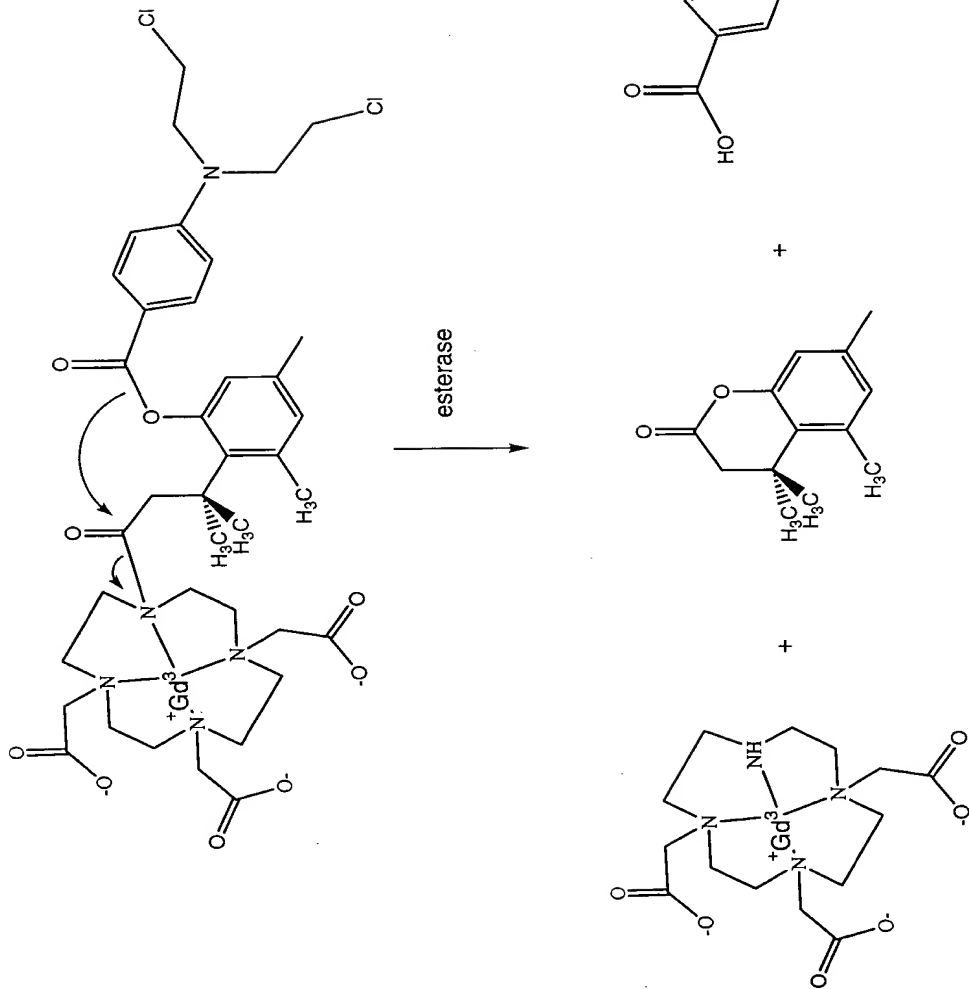
F⁺ (Acetoxy)alkoxy Linker

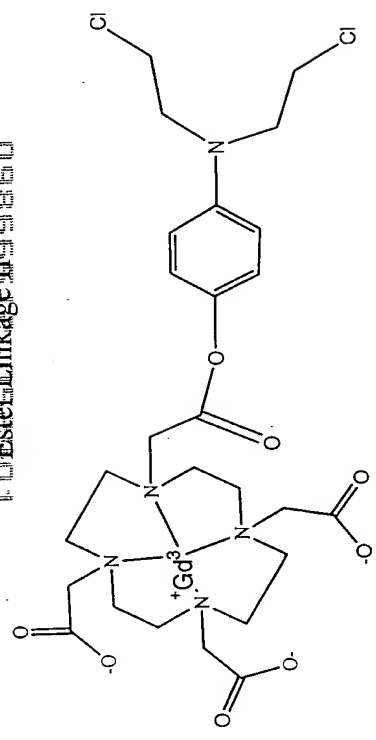
Fig 20A B



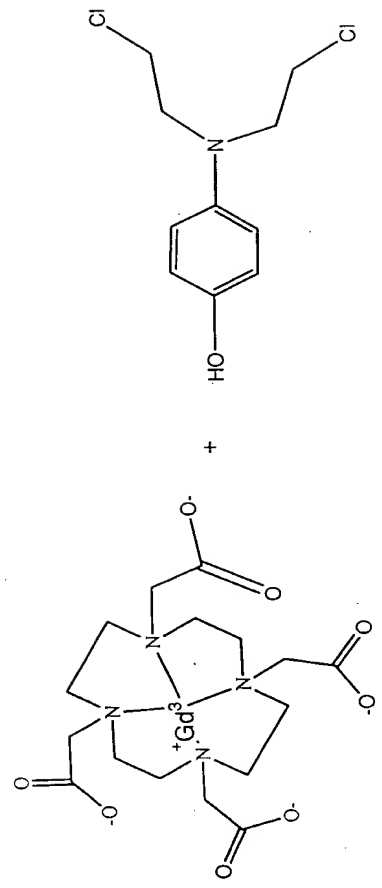
esterase







esterase
↓



Fmoc Chemistry for Synthesis of Linker-peptide unit

I.

MBHA Rink Amide Resin

or

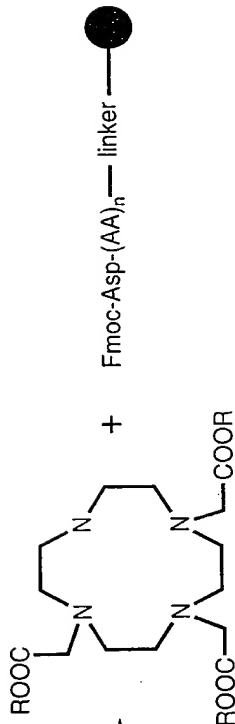
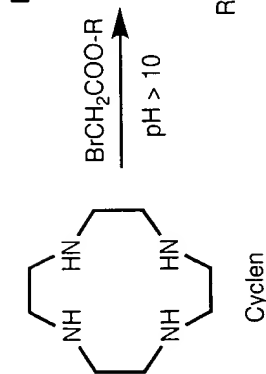
PAL-PEG-PS Resin

Activation with 20% piperidine
in DMF

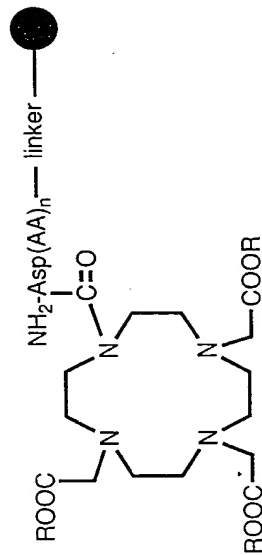
Fmoc AA-OH/HOAt/HATU/DIEA

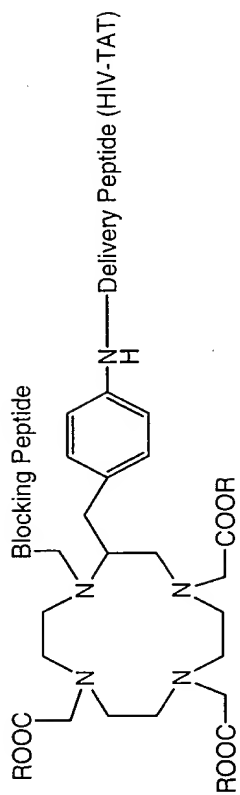
1. N-ε-Fmoc-ε-amino-R acid
[H₂C(CH₂)_x-NH-Fmoc]
2. Fmoc-AA-OH
3. Fmoc-AA-OH
4. (Fmoc-AA-OH)_n
5. Fmoc-Asp-OH

II.



III.





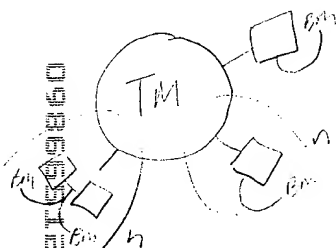
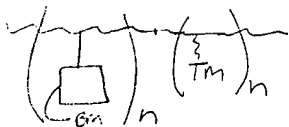
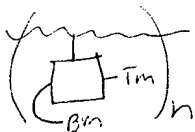
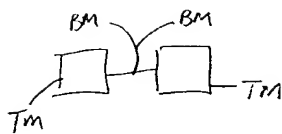
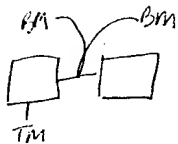
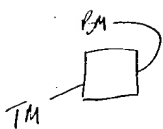


Fig 23